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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/724,225	12/01/2003	Bruno Tocque	ST95050-US/A	9762
29693	7590	04/22/2005	EXAMINER	
WILEY, REIN & FIELDING, LLP ATTN: PATENT ADMINISTRATION 1776 K. STREET N.W. WASHINGTON, DC 20006			EPPS FORD, JANET L	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 04/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/724,225

Applicant(s)

TOCQUE ET AL.

Examiner

Janet L. Epps-Ford, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/01/03.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 December 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☒ Certified copies of the priority documents have been received in Application No. 09/029,327.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>5-19-04</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Priority

1. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence(s) of the specification or in an application data sheet by identifying the prior application by application number (37 CFR 1.78(a)(2) and (a)(5)). If the prior application is a non-provisional application, the specific reference must also include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Drawings

2. New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because the labels on the X-axis of the graph set forth in Figure 3a are illegible. Applicant is advised to employ the services of a competent patent draftsman outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 1, line 5, and those claims dependent therefrom, recite the phrase “whereby a p53 polypeptide or fragment and exhibiting a reduced cell growth level.” This phrase is vague and indefinite, the skilled artisan would not be able to apprise what Applicant’s invention is, or how to practice it.

6. Claim 1 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: A final step that correlates the recited method steps with the preamble, particularly wherein the recited steps actually allows the skilled artisan to determine the mdm-2 dependent growth activity of a cell. The final 2 lines of the claim suggests that the method is drawn to a method of inhibiting a transforming property of mdm2, however there are no steps that conclude with a determination of mdm-2 dependent growth activity of a cell.

7. Claims 6, and those claims dependent therefrom, are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is a step that correlates the binding recited in the last line of this method with detection of a protein-protein interaction with a mdm2 protein, as recited in the preamble. The method comprises expressing in the cell a

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mdm2 protein and a cell cycle regulatory protein, and in the last step of the method it recites that “whereby a change in cell growth or proliferation is indicative of binding to mdm2.” However, there is no indication that the binding recited in the last step of this method represents binding of the cell cycle regulatory protein with mdm2, the generic recitation of the term “binding” may encompass binding of any cellular component with mdm2, not just binding of proteins to mdm2.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burrell et al. (WO 93/20238 A2).

Although the methods recited in claims 1-10 are considered vague and indefinite for the reasons set forth above, the following prior art is applied to the extent that the claims are interpreted as encompassing 1) a method for determining mdm2-dependent growth activity of a cell comprising introducing a nucleic acid encoding mdm2 protein and introducing a vector for expressing a p53 polypeptide or fragment in the same cell, wherein if a reduced cell growth is observed in comparison to a control, then the p53 polypeptide or fragment thereof is capable of inhibiting mdm2-dependent growth activity of a cell (claims 1-5); 2) A method of detecting protein-protein interaction with a mdm2-protein comprising expressing a mdm2 protein and a p53 protein in a cell and observing a change in cell growth or proliferation in said cells, whereby a change in cell growth or proliferation indicates binding of p53 to mdm2 (claims 6-11). Note

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again that the instant prior art is applied based upon the examiner's interpretation of what Applicants intended the claims to encompass.

Burrell et al. teach that human MDM2 is over expressed in some neoplastic cells and the expression of MDM2 encoded products are also correspondingly elevated in tumors. Burrell et al. also teach that MDM2 is significantly amplified in liposarcomas and osteocarcinoma (see page 19, 4th paragraph). The sequence of amino acid MDM2 as set forth in amino acids 1 to 134 of SEQ ID NO: 1 is set forth in Burrell et al. at Figures 1A-1C. The elevated levels of MDM2 appear to sequester p53 and allow the cell to escape from p53-regulated cell growth (see page 5, 6th paragraph), leading to tumorigenesis (see page 12, 4th paragraph). Burrell also teach a method for inhibiting the growth of tumor cells wherein MDM2 expression is amplified, wherein said method comprises administering to the tumor cell a DNA encoding an MDM2 binding, p53-derived peptide, wherein said peptide competes with wild-type p53 for binding to MDM2, and functions to alleviate the sequestration of wild-type p53 by MDM2, leading to the re-establishment of p53-regulated growth control (see page 11, 3rd paragraph). In particular, Burrell et al. teach that amino acid residues 13-41 of p53 are necessary for the interaction of MDM2 and p53 (page 11, 3rd paragraph).

Although Burrell et al. does not teach the exact method steps recited in the instant claims, it is clear that one of ordinary skill in the art at the time of the instant application, seeking potential therapeutics for treating MDM2 associated neoplastic cell growths, would have been motivated to modify the teachings of Burrell et al. to design the methods recited in the instant claims. One of ordinary skill in the art at the time of the instant invention would have been motivated to make this modification since Burrell et al. clearly teach that potential therapeutic

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molecules can be identified by identifying molecules which inhibit the binding of MDM2 to p53, and further determining whether this inhibition alleviates p53 sequestration (see page 11, lines 1-2), with the expectation that p53 regulated cell growth control would be restored (see page 11, 3rd paragraph). Moreover, one of ordinary skill in the art seeking alternative means for isolating inhibitors of MDM2 function would have been motivated to practice the methods of the instant invention in saos-2 cell, since Burrell et al. specifically teach that MDM2 is amplified in osteosarcomas (see page 19, 4th paragraph), and since saos-2 cells are osteosarcoma cells, it would have been obvious at the time of the invention to substitute one functionally equivalent cell line with another, with the expectation that MDM2 would also be amplified in saos-2 cells as the prior art cells.

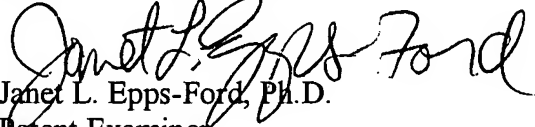
Therefore, the invention as a whole would have been *prima facie* obvious over Burrell et al.

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10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Janet L. Epps-Ford, Ph.D.
Patent Examiner
Art Unit 1635

JLE